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B2

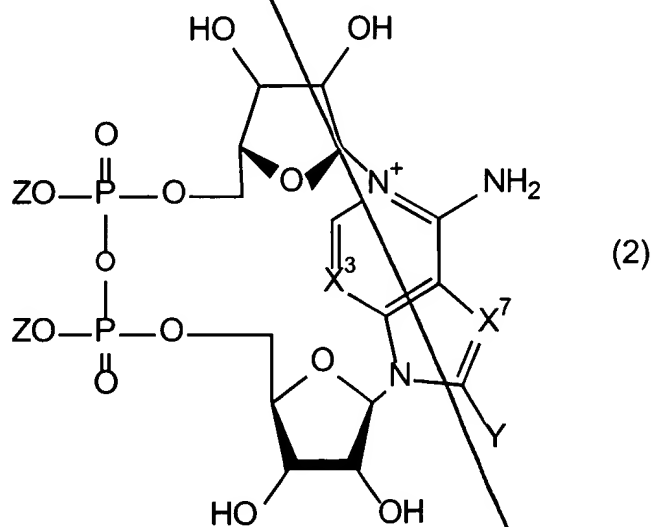
1. A method for modulating T cell activation *in vivo* or *ex vivo* in a mammal comprising administering to the mammal or a mammalian T cell culture an effective amount of a compound capable of antagonizing a sustained cADPR-mediated rise in intracellular Ca^{2+} levels in a T cell, said rise being in response to stimulation of the T cell receptor/CD3 complex of the T cell.

2. A method according to claim 1 wherein the compound modulates the binding of cADPR to a ryanodine receptor/ Ca^{2+} channel.

3. A method according to claim 1 wherein the compound is a cADPR analogue.

4. A method according to claim 3 wherein the compound comprises an adenine component to which is individually linked two ribose moieties or a derivative(s) thereof, which ribose moieties are joined via a pyrophosphate bridging group.

5. A method according to claim 3 wherein the compound has the formula (2):



wherein:

X³ is independently either CR¹ or N;

X⁷ is independently either CR² or N;

Y is selected from the group consisting of halo, C₁ to C₂₀ hydrocarbyl, N(R³)(R⁴), OR⁵, SR⁶ nitro and carboxyl, wherein each of R¹, R², R³, R⁴, R⁵ and R⁶ is independently either H or C₁ to C₂₀ hydrocarbyl; and

Z is independently selected from the group consisting of H, a caging group, a bio-isostere, and a pharmaceutically acceptable salt thereof.

8. A method according to claim 10 wherein the patient has a graft rejection or an autoimmune disease selected from the group consisting of thyroiditis, insulinitis, multiple sclerosis, iridocyclitis, uveitis, orchitis, hepatitis, Addison's disease, myasthenia gravis, rheumatoid arthritis and lupus erythematosus.

15. A compound identified by a method of claim 17.

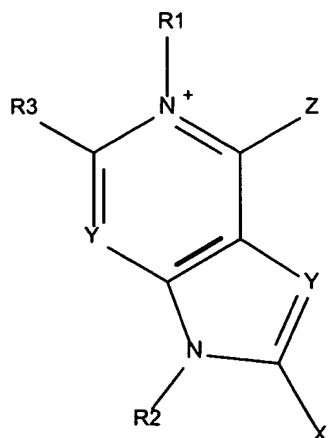
Please cancel claims 6, 7, 9 to 14, and 16 to 18 and add the following new claims

19 to 31:

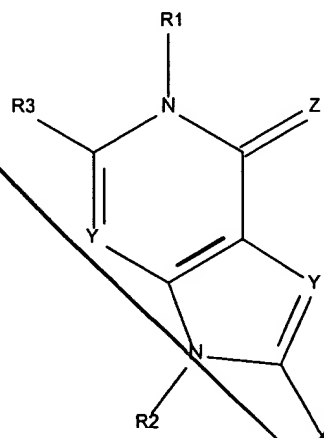
19. A method according to claim 1 wherein the compound is 7-deaza-8-Br-cADPR or 8-Br-cADPR.

20. A method according to claim 1 wherein the compounds have either formula (3) or (4):

Formula (3)



Formula (4)



wherein, for formula (3), Z is selected from the group consisting of OH, OR, SH, SR⁶, NH₂ and NHR¹R² and, for formula (4), Z is selected from the group consisting of O, S, NH and NHR¹; and wherein for either formula (3) or formula (4),

5 Y is either N or CH;

X is selected from the group consisting of halo, NH₂ or NHR¹R²;

R₁ and R₂ are independently selected from the group consisting of H, C₁ to C₂₀ hydrocarbyl, sugar moieties and phosphate groups; and

10 R₃ is selected from the group consisting of H and C₁ to C₂₀ hydrocarbyl, a bio-isostere, and a pharmaceutically acceptable salt thereof.

21. A method according to claim 1 which modulates the immune response in the mammal.

22. A method according to claim 1 wherein T cells are removed from a mammalian patient, treated with the compound, and then returned to the patient.

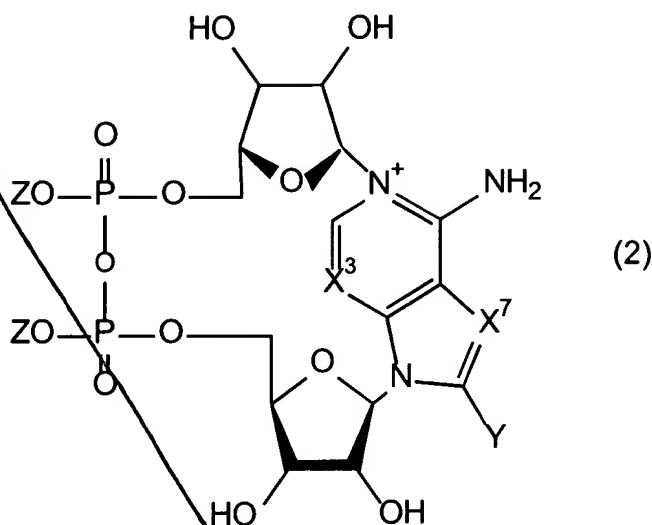
23. A method of treating a human or animal patient suffering from an immune disorder which method comprises administering to the patient an effective amount of a compound capable of antagonizing a sustained cADPR-mediated rise in intracellular Ca²⁺ levels in a T cell, said rise being in response to stimulation of the T cell receptor/CD3 complex of the T cell, such that T cell activity is modulated.

24. A method according to claim 23 wherein the compound modulates the binding of cADPR to a ryanodine receptor/Ca²⁺ channel.

25. A method according to claim 23 wherein the compound is a cADPR analogue.

26. A method according to claim 25 wherein the compound comprises an adenine component to which is individually linked two ribose moieties or a derivative(s) thereof, which ribose moieties are joined *via* a pyrophosphate bridging group.

27. A method according to claim 25 wherein the compound has the formula (2): formula (2):



wherein:

X^3 is independently either CR^1 or N;

X^7 is independently either CR^2 or N;

Y is selected from the group consisting of halo, C_1 to C_{20} hydrocarbyl, $N(R^3)(R^4)$, OR^5 , SR^6 nitro and carboxyl, wherein each of R^1 , R^2 , R^3 , R^4 , R^5 and R^6 is independently either H or C_1 to C_{20} hydrocarbyl; and

Z is independently selected from the group consisting of H, a caging group, a bio-isostere, and a pharmaceutically acceptable salt thereof.

28. A method according to claim 27 wherein the patient has rheumatoid arthritis.

29. A method for identifying a substance capable of modulating a sustained rise in Ca^{2+} entry *via* a cADPR-mediated pathway which method comprises either:

(i) contacting an ADP-ribosyl cyclase or a homologue, variant or derivative thereof, with a substance to be tested under conditions that would permit the synthesis of cADPR in the absence of the substance, and determining whether the substance affects cADPR synthesis; or